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## Obviousness-Type Double Pat nting Rejection

In the July 1, 2003 Office Action, the Examiner rejected claims 74-92 under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-22 of U.S. Patent No. 6,046,005 in view of Arbo et al. (International Journal of Peptide and Protein Research, (1993), Vol. 42, pages 138-154) further in view of Liu et al. (Anal. Chem. (2000), Vol. 72, pages 33030-3310). The Examiner then set forth the reasons for the obviousness-type double patenting rejection essentially as detailed in the Office Action issued March 4, 2003 in connection with the above-identified application. The reasons are not repeated here for reasons of brevity.

The Examiner further stated, in response to the arguments made by applicants in their Communication filed June 4, 2003, that applicants' arguments with respect to all pending claims have been considered but are they are not persuasive. The Examiner stated that applicants argue that the obviousness-type double patenting rejection should be withdrawn because the Arbo et al. reference does not teach a linker which is a derivative of 4aminomethyl benzoic acid containing fluorine and the linker taught by the Arbo reference is a "very weak coordinating anion". The Examiner stated that this argument is not persuasive for two reasons. First, the "comprising" language of claim 74 allegedly permits any additional step(s) or material(s) to be added in any order with the claimed method. The Examiner stated that although the chemical moiety disclosed by Arbo (trifluoromethane sulfonic acid) associated with non-fluorine containing 4-aminomethyl benzoic acid-based molecule, it meets the claim language because it "comprises" both the 4-aminomethyl

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benzoic acid and fluorine moieties. Second, in response to applicants' argument that the reference fails to show certain features of applicants' invention, the Examiner noted that the features upon which applicants rely (i.e., not "very weak coordinating anion" or "very strong coordinating anion") are not recited in the rejected claim(s). The Examiner stated that although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims.

The Examiner further deemed unpersuasive applicants' argument that Liu et al. does not teach a channel whose surface is coated with a compound that specifically interacts with a chemical moiety, nor does it teach a channel connected to a well at each end, and step (e) of claim 74. The Examiner stated that Liu et al. clearly teaches a channel whose surface is coated with a compound (Acrylic-polyester based Casolite AP and Epofix resins in this case) that specifically interacts with a chemical moiety well known in the art, and also teaches a channel connected to a well at each end (figure 2 and page 3305, column 1). The Examiner further stated that regarding teaching of step (e) of claim 74, it was clearly mentioned in the previous office action that Ju et al. teaches freeing the DNA sequencing fragment from the surface by disrupting and cleaving the interaction between the chemical moiety attached via the linker to the DNA sequencing fragment and the compound on the surface (claims 1 and 15 and Experimental Section and figures 9-10).

The Examiner further stated that applicants' position of non-obviousness is not persuasive.

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The Examiner stated that first, in response to applicants' argument against the references individually, one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. The Examiner also stated that it has been clearly demonstrated in the response to arguments as described above and in the last Office Action that every element of the claims has been either taught or suggested by the cited references. The Examiner stated that second, clear motivation has been provided by Liu et al. since it states, "Considering the wide acceptance of the microtiter well plate format in automated analysis and the potentially low cost of plastic devices, a disposable device equipped with an independent electrospray exit port for each sample well represents an attractive alternative to FIA (page 3304, column, 1, lines 6-10)." The Examiner also stated that Liu et al. provides further motivation as Liu et al. states "Nevertheless, the model application demonstrates the potential of automated analysis with the present device design (page 3309, column 1, last sentence of the second paragraph)". The Examiner stated that similar strong motivations have been provided by other references as well. The Examiner stated that third, with regard to lack of "reasonable expectation of success" argument, there is no evidence of record submitted by applicants demonstrating the absence of a reasonable expectation of success. The Examiner stated that there is evidence in the Ju reference of the enabling methodology, the suggestion to modify the prior art, and evidence that Ju et al. teach a method for sequencing several DNA by identity of detecting the a single orplurality dideoxynucleotide incorporated to the 3' end of a DNA sequencing fragment using mass spectrometry (Abstract and claims 1, 14, and 15, figure 1 and Experimental Section). The Examiner stated that

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this evidence of functionality trumps the attorney arguments since Ju steps beyond research and shows the functional product.

In response, applicants respectfully traverse the Examiner's rejection.

Applicants assert that the invention claimed in the '005 patent in view of Arbo et al. and Liu et al. do not teach all the elements of the claimed invention. Moreover, the other references cited by the Examiner do not cure this deficiency.

Specifically, applicants note that Arbo et al., contrary to the Examiner's assertion, does not teach or suggest a linker containing fluorine which is a derivative of 4-aminomethyl benzoic acid, as shown in claim 74. Arbo et al. teaches a linker molecule, but this linker molecule does not contain fluorine. Applicants further note that the mere presence of a separate fluorine-containing anion (which itself is not a linker), as disclosed in Arbo et al., does not anticipate a fluorinecontaining linker. More particularly, none of the fluorine containing linker structures shown in claim 74 are taught by Arbo et al. In addition, applicants wish to make it clear that contrary to the Examiner's statement that applicants argue "the linker taught by [the] Arbo reference is a 'very weak coordinating anion'", applicants have never made a statement that the anion is a linker, and, in fact, have distinguished between the linker molecule and the anion, as Arbo et al. does in the figure on page 138, which shows the linkers alone.

Applicants also note that the Examiner's position that the "comprising" language of claim 74 permits the TFMSA anion

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associated with the non-fluorine-containing 4-aminomethyl benzoic acid disclosed in Arbo et al. to anticipate the fluorine-containing linker molecules shown in claim 74 is erroneous. Claim 74 clearly states that the linker is selected from a group consisting of illustrated structures, all fluorine-containing linker molecules, none of which are taught by Arbo et al. Applicants note that unless Arbo et al. teaches or suggests the fluorine containing structures shown in claim 74, it does not make claim 74 obvious regardless of the "comprising" language.

Finally, applicants note that Liu et al. does not teach a channel whose surface is coated with a compound that specifically interacts with a chemical moiety, nor does it teach a channel connected to a well at each end, as cited in step (c) of claim 74. The remaining cited references do not cure this deficiency. Specifically, the well plate disclosed by Liu et al. does not teach a coated surface. The Examiner states that the Epofix resin (or other resin) is the coating. In fact, as stated in Liu et al. at page 3304, under the heading "Fabrication of the Multisprayer Device", and as shown in figure 1 legend and figure 2 legend, the Epofix resin is the very material from which the well itself is made, not a surface coating. Furthermore, the Examiner's citation of Liu et al. teaching a channel connected to a well at each end (page 3305, column 1) in fact teaches a channel connected to a well at one end and an electrospray port at the other end (see also figure 1 of Liu et al. for a cut-away drawing of the apparatus). Indeed, Liu et al. itself clearly distinguishes between the well element and the electrospray port element when it refers to both elements in the same sentence later cited by the Examiner, namely "a disposable device equipped with an independent electrospray port for each sample well..", page 3304,

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Col. 1, lines 6-10.

Applicants thus maintain that the instant claims are not obvious under the doctrine of obviousness-type double patenting, over the '005 patent, in view of Arbo et al. and Liu et al. Accordingly, applicants request that the Examiner reconsider and withdraw this ground of rejection.

## Rejection of Claims Under 35 U.S.C. §103(a)

The Examiner rejected that claims 74-92 under 35 U.S.C. §103(a) as being anticipated by Ju et al., U.S. Patent 6,046,005 (April 4, 2000) in view of Arbo et al. (International Journal of Peptide and Protein Research, (1993), Vol. 42, pages 138-154) further in view of Liu et al. (Anal. Chem. (2000), Vol. 72, pages 3303-3310). The Examiner then set forth the reasons for the rejection under 35 U.S.C. §103(a) essentially as detailed in the Office Action issued March 4, 2003 in connection with the above-identified application, which will not be repeated here for reasons of brevity.

In response to the Examiner's rejection, applicants respectfully traverse, and maintain that the Examiner has failed to establish a prima facie case of obviousness. Specifically, applicants assert that the '005 patent, in view of Arbo et al. and Liu et al. do not teach all the elements of the claimed invention. In support of this position, applicants direct the Examiner to the discussion of the teachings of the '005 patent, Arbo et al. and Liu et al. set forth above in connection with the obviousness-type double patenting rejection.

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Applicants maintain that the claimed invention is not obvious over the '005 patent, in view of Arbo et al. and Liu et al. Accordingly, applicants request that the Examiner reconsider and withdraw this ground of rejection.

## Summary

Applicants maintain that the claims pending are in condition for allowance, and accordingly, allowance is respectfully requested.

If a telephone interview would be of assistance in advancing prosecution of the subject application, applicants' undersigned attorneys invite the Examiner to telephone them at the number provided below.

No fee is deemed necessary in connection with the filing of this Communication. If any fee is required, however, authorization is hereby given to charge the amount of any such fee to Deposit Account No. 03-3125.

Respectfully submitted,

hereby certify that this correspondence is being deposited this date with the U.S. Postal Service with sufficient postage as Postal first class mail in an envelope addressed to: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 223/13-1/450

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1/03

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